# Meshed *tert*-Butyl Gears on a Quasirigid Backbone

**ANATOLY M. BELOSTOTSKII*, ALFRED HASSNER**

*Chemistry Department, Bar-Ilan University, Ramat-Gan 52900, Israel*

*Received 11 March 1998; accepted 29 July 1998*

**ABSTRACT:** MM3-based calculations showed that bicycles and polycycles with four- to six-membered rings-components of the bi- and polycyclic backbone are sufficiently rigid to keep a syn-periplanar orientation of vicinal *tert*-butyl substituents. As a result of the spatial proximity of these groups, their rotation occurs in a concerted manner as demonstrated by conformational schemes that are built using MM3-derived methodology. Only correlated disrotation in saturated systems with four- to five-membered rings-components and in the adamantane system leads to isochronism for Me groups of the *tert*-Bu substituents (i.e., to dynamic gearing in Mislow's terms). Moreover, correlated rotation of these substituents is coupled with a change of the backbone geometry (pseudorotation) except in the most rigid bicyclo[2.1.1]hexa-2-ene system. Thus, a new type of dynamic gearing, correlated rotation–rotation–pseudorotation, is predicted for quasirigid bi- and polycycles with syn-periplanar oriented *tert*-Bu substituents. © 1998 John Wiley & Sons, Inc. J Comput Chem 19: 1786–1794, 1998

**Keywords:** gear effect; internal rotation; molecular mechanics; MM3 force field; hindered systems

## Introduction

The accepted definition of the ''gear effect'' as ''a conformational transmission, which is caused by interaction between polyhedral substituents and which depends on their polyhedral shape,''[1–3] does not specify which intramolecular motions are meshed by this transmission. What are considered by this expression are correlated rotations of molecular fragments,[1–5] while other coupled processes like possible concerted NIR-NIR (NIR = nitrogen inversion and C–N rotation[6–8]) in *N*,*N*′-disubstituted bicyclic hydrazines[9,10] are not considered. Furthermore, only synchronized *disrotation* of a pair of meshed molecular rotors was introduced by Mislow and colleagues[4,11] as ''dynamic gearing,'' which is based on a direct analogy with mechanical gears. From this point of view,

*Correspondence to:* A. M. Belostotskii; e-mail: belostot@mail.biu.ac.il

Contract/grant sponsor: Eliezer Giladi–Benjamin Fein government program



CCC 0192-8651 / 98 / 151786-09

concerted conrotation of the ortho substituents in *o*-di-neopentylbenzene[2,12] does not belong to dynamic gearing. Mislow mentioned that this analogy is limited in part because of ''the rubbery nature of chemical rotors.''[4] In other words, rotation and thus concerted rotation are generally accompanied by other intramolecular motions (e.g., see ref. 13). Nevertheless, excluding the slippage features of molecular dynamic gearing,[4] this type of conformational dynamics is still considered to be within the limits of concerted rotation only.[1,5] Herein, by means of a molecular mechanics (MM) approach using the MM3 force field, we describe models for a dynamic gearing for which other rotation-coupled motions cannot be neglected.

The *tert*-butyl groups were accepted as insufficient rotors for net dynamic gearing in Mislow's terms[4] (i.e., the lowest energy conformational pathway for interchange of Me groups is not accomplished via concerted disrotation only). For instance, both conrotation and disrotation are involved in this interchange for di- and tri-*tert*-Bu methanes (bevel gears[4]).[14,15] Nevertheless, this bulky symmetrical group seems attractive to us as a simple molecular gear that in some cases is capable of net dynamic gearing. Relatively rigid backbones of compounds **1**–**10** (see Table I) permit a prediction of the proximity of vicinal *tert*-Bu substituents in **2**–**10** and the remoteness of those groups in **1**. Therefore, we performed a MM3-based study of conformational dynamics for these models to find positively meshed *tert*-Bu gears.

## Results and Discussion

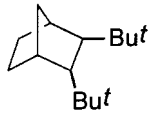
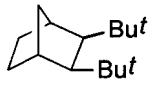
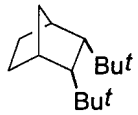
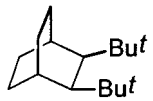
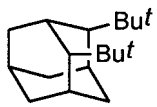
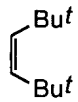
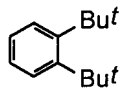
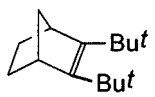
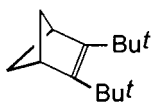
Our MM3 package based methodology consists of finding stable conformations and transitions states and establishing the formal relationship between stable conformations and transition states (i.e., the design of a conformational scheme).[16] A MM3-assisted stochastic conformational search was performed in order to build a scheme for each model compound (this search proved to be reliable for the NIR studies of open chains, as well as cyclic compounds[7,8]). Furthermore, the *tert*-Bu group rotation procedure (see the Experimental section for details) was used independently to prove whether the all *tert*-Bu rotation transition states were found via the stochastic search. The results of the conformational search provided a set of stable conformations and transitions states. Rotation of one *tert*-Bu group, as well as simultaneous rotation of two *tert*-Bu groups, also led to a set of maximum and minimum energy points. Geometry optimization (by the MM3 full matrix minimization option) of these points gave a set of transition states and stable conformers. Normal mode vibrational analysis (supported by the MM3 package) was used to establish the relationship between stable conformations and transition states that were obtained via the conformational search and the rotation procedure (see also ref. 16). Thus, these relationships provide a comparison of the geometry for the conformers that are separated by only related transition state(s).

It should also be noted that MM3-assisted rotation turned out to be ineffective in some of the cases studied. At a certain stage the forced *tert*-Bu rotation causes a severe change of the backbone structure due to the coupling of rotation with pseudorotation (PSR; see below). This forced rotation is continued starting from *another* conformation as indicated by fractured lines in the rotation maps. Nevertheless, at least in the case of adamantane derivative **6**, the transition state was found by the rotation procedure (the cage boundary of **6** does not permit a necessary spatial reorganization for most of the stochastically generated arbitrary structures via their energy minimization). Also, for the relatively rigid bicycle **9** the rotational procedure turned out to be necessary because the conformational energy surface of **9** possesses multiple maxima and minima, and establishment of conformational itineraries via stochastic search only becomes too laborious and unreliable.

As expected, isolated rotation (ISR) was only found for the remote *endo*- and *exo*-*tert*-Bu groups of **1**. The barrier values are 5.2 and 5.6 kcal/mol for rotation of the *endo*- and *exo*-*tert*-Bu groups, respectively. The calculated angle $\Theta$ between the *tert*-Bu group rotation axes (i.e., between $CMe_3$–C bonds; see Table I for the values) in the lowest energy conformation of **1** is 113.4° while $\Theta$ is lower than 32.4° for saturated analogs **2**–**6**. Deviation from a midplane of the *tert*-Bu substituents in **7**, **9**, and **10** is also not significant (see $\Theta$ values). Thus, *tert*-Bu rotor shapes in vicinal systems **2**–**5** and **7**–**10**, as well as in diaxial system **6**, are proximal and orientation of the rotation axes is nearly parallel (excluding compounds **5** and **8**). This indicates a possibility for ''friction'' of these groups during rotation in **2**–**10**.

Indeed, for compounds **2**–**9** rotation of both the *tert*-Bu groups is found to be correlated and coupled with a notable change of a) the dihedral angle between vicinal *tert*-Bu groups and b) the internal

**TABLE I.**
**Intramolecular Dynamic Processes and Corresponding Barriers (kcal / mol) for Compounds 1–10.**

| Entry | Structure | Θ | PSR–ISR–ISR | Dynamic Gearing |
|---|---|---|---|---|
| **1** |  | 113.4° | — | – |
| **2** |  | 13.2° | 11.1 (disrotation) | + |
| **3** |  | 3.5° | 8.7 (distrotation) | + |
| **4** |  | 6.8° | 1.9 (conrotation)<br>9.3 (disrotation) | + |
| **5** |  | 32.4° | 3.2 (conrotation)<br>9.6 (disrotation)<br>11.9 (disrotation) | – |
| **6** |  | 6.4° | 6.9 (disrotation) | + |
| **7** |  | 4.9° | 2.4 (disrotation)<br>3.0 (conrotation) | – |
| **8** |  | 38.5° | 4.0 (disrotation)<br>5.6 (conrotation) | – |
| **9** |  | 2.6° | 1.1 (disrotation)<br>1.1 (disrotation) | ±[a] |
| **10** |  | 0.4° | 2.9 (disrotation)[b] | + |

The calculated energies relative to the lowest energy stable conformer are shown. No other processes excluding those shown in the table and footnotes were found for compounds **1**–**10**. ISR barriers for the *exo*- and *endo*-*tert*-Bu groups of **1** are 5.6 and 5.2 kcal / mol, respectively.

[a] ISR barrier = 1.7 kcal / mol.

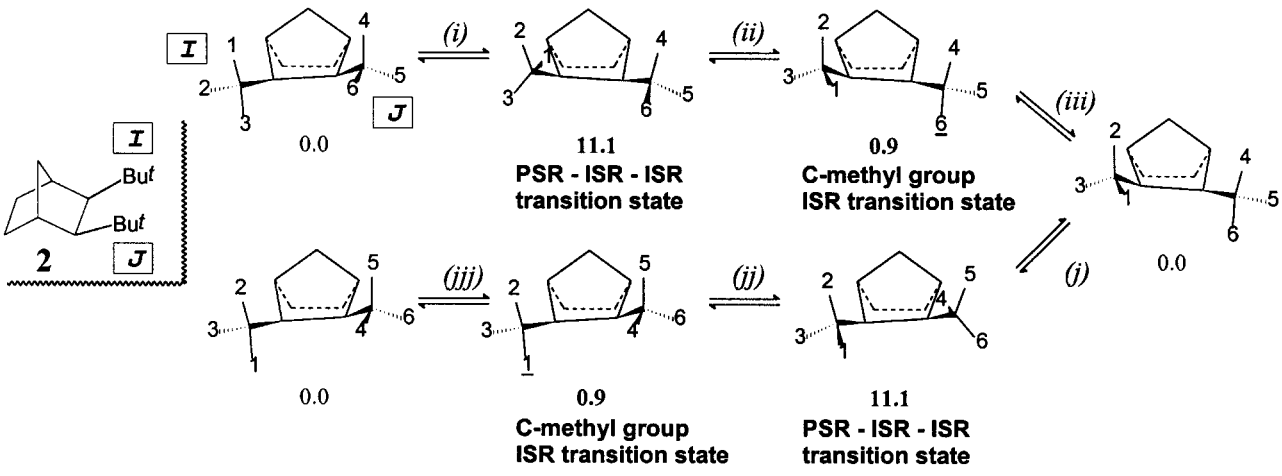
[b] For ISR–ISR.

torsion angles of the di-*tert*-Bu substituted ring (see Schemes 1–3, Table I). For instance, the C(3)–C(2)–C(1)–C(7) and C(2)–C(3)–C(4)–C(7) dihedral angles of bicycle **2** ''interchange'' their absolute values (29.8° and 39.7°) during the one step *stable conformer–stable conformer* transformation (one-half of the pathway in Scheme 1). Two dihedral ring angles of the aromatic system **8** undergo a similar value interchange even with a bigger amplitude (11.2° to −11.2° and −11.2° to 11.2°). For compounds **3**–**9** the change of the analogous endocyclic torsion angles is significantly less (ca. 2–5°). Thus, even in the case of **2** the geometry perturbation during the one step transformation (''rocking'' of the boat component of the bicyclic skeleton, see Scheme 1) is less obvious than that for the boat–twist transformation in six-membered monocycles (achieved via PSR[17]).

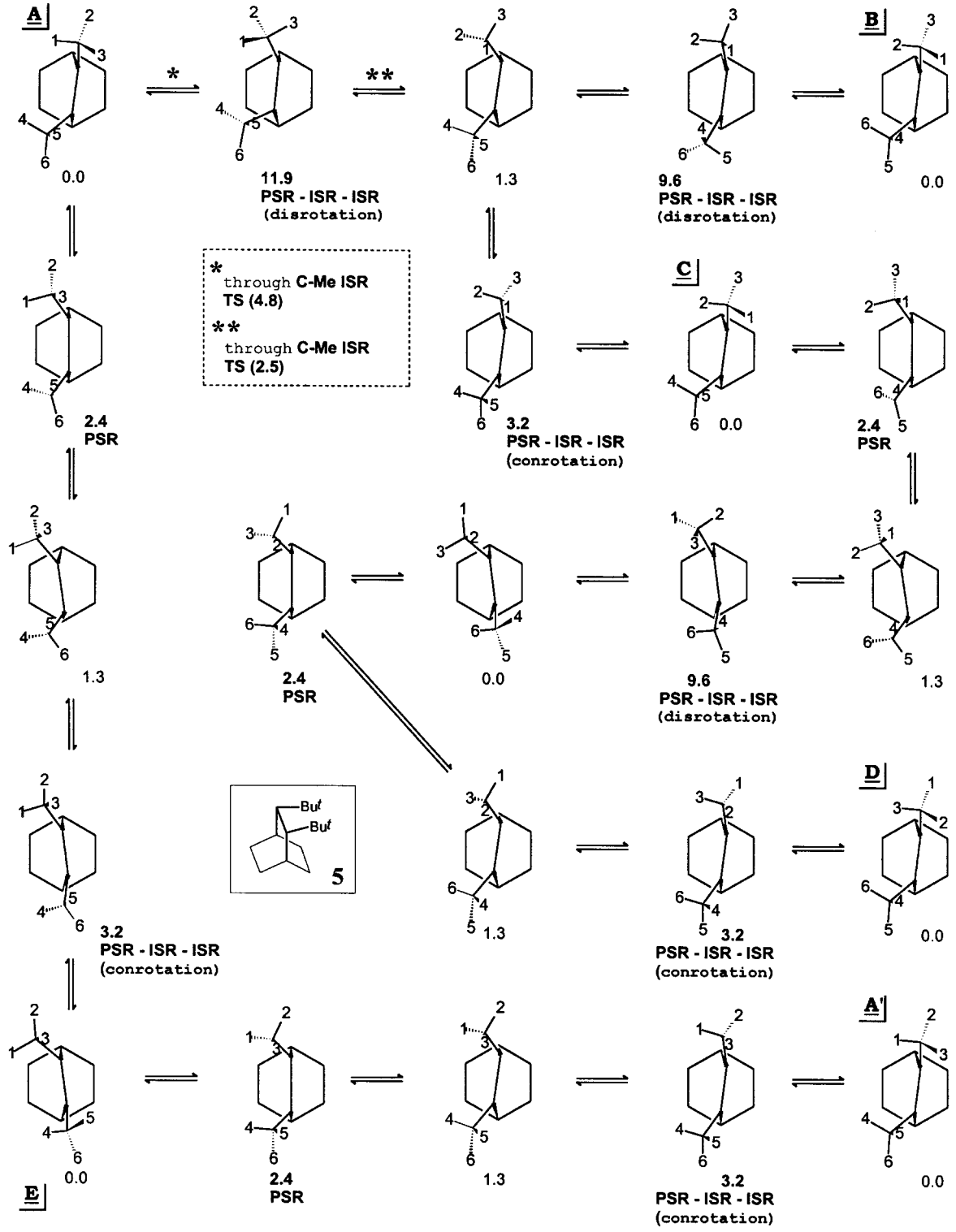
However, this change cannot be ignored. The coupled *tert*-Bu rotation and backbone rocking leads to a complete structure inversion for **2**–**4** and **6**–**9**. Even cage structure **6** is distorted in the stable conformation and is inverted via this process. It is also obvious that structural inversion in rigid bi- or polycyclic systems, if it exists, is not capable of causing significant structural distortions like those for monocyclic analogs.[17–19] In the more flexible system **5** disrotation causes a twist–boat transformation (known as PSR for six-membered monocycles[17] or defined as bicyclic ring torsion for an analog of **5**, 2,3-diazabicyclo[2.2.2]octane system[20]) for all three rings and components of the bicyclic skeleton (see below). Therefore, we prefer to characterize the rocking for compounds **2**–**9** as PSR according to an analogy with a limited change of internal dihedral angles in four- to six-membered saturated rings. Such a change in dihedral angles is also not significant for PSR in essentially flattened monocycles.[21] For the open chain system **7**, PSR means a sign inversion for the Θ value.

The conformational scheme for compound **2** reflects in general a PSR − *tert*-Bu concerted disrotation process for saturated cycles **3**, **4**, and **6** (the C–Me rotation transition state is a similar component of the conformational scheme only for *endo*-substituted isomer **3** with the barrier of 2.5 kcal/mol). In the stages (i)–(iii) (Scheme 1) the major rotation belongs to the *tert*-Bu group ***I*** (ca. 116°) while group ***J*** is rotated only ∼ 14°. In the stages (j)–(jjj) group ***I*** undergoes a minor 14° rotation and a major 116° rotation belongs to group ***J***. Thus, isochronism of Me groups, as well as of the corresponding backbone and exocyclic quartenary atoms, is achieved by a triple intramolecular motion, concerted PSR–*tert*-Bu rotation–*tert*-Bu rotation while *tert*-Bu substituents undergo disrotation only.

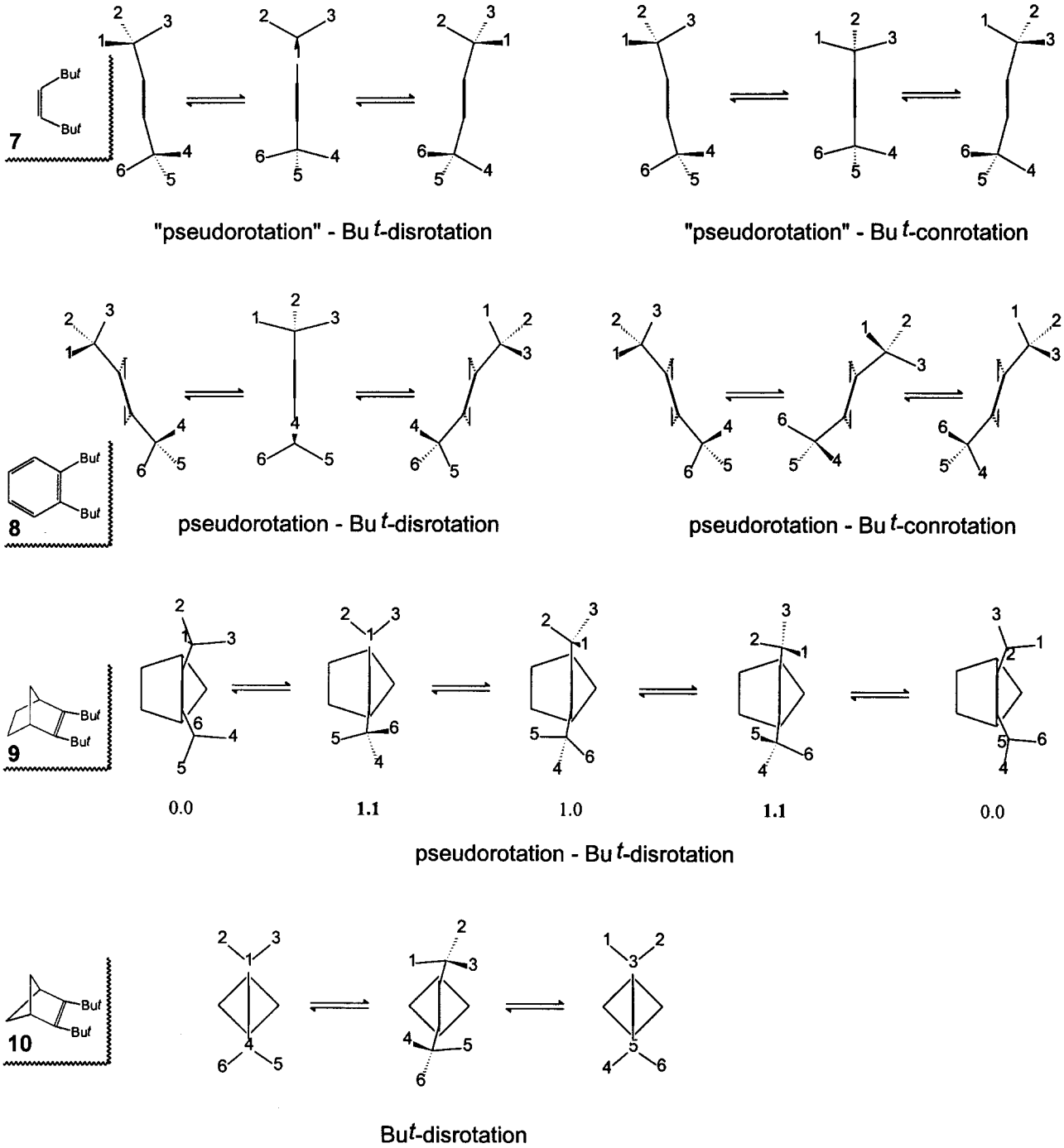
This triple *disrotation*-coupled motion is the highest energy process for Me group interchange for the more flexible bicycle **5** (Scheme 2, the **A** → **B** transformation). A lower energy positional exchange of these groups (the **C** → **D** transformation) is achieved via three motions: 1) a triple process (i.e., PSR − *tert*-Bu rotation − *tert*-Bu rotation) with *conrotation* of these substituents, 2) PSR (*twist–distorted boat* transformation of the ring components of **5** without substituent rotation with a change of endocyclic dihedral angles of ∼ 8–10°), and 3) a triple process with disrotation. The low




**SCHEME 1.** Conformational scheme for the positional interchange of the Me groups for compound **2**; the Me groups are depicted by the numbers. Relative energies of stable conformations and transition states are in bold (kcal / mol).




**SCHEME 2.** Conformational pathways for the Me group interchange for compound **5** (TS, transition state). Energies (kcal / mol) are relative to the lowest energy conformer. The values for the transition states are shown in bold. The Me groups are depicted by the numbers.




**SCHEME 3.** Conformational transformations in unsaturated compounds **7**–**10**. The pathways *stable conformer–transition state–stable conformer* are shown keeping a midplane orientation; the Me groups are depicted by the numbers. The itinerary of the Me group interchange is given for olefin **9** with nonequivalent *tert*-Bu groups in the lowest energy conformation; barrier values (kcal / mol) are in bold. Distortions of the bicyclic backbone for **9** on this pathway are not shown.

energy itinerary that includes conrotation-coupled PSR and PSR (**A** → **A**′ transformation via structure **E**) leads only to chemical equivalency of the quaternary carbon atoms and to equivalency for the pairs of the Me substituents from the vicinal *tert*-Bu groups (compare structures **A** and **E**). Thus, in spite of the coupling of intramolecular motions, compound **5** does not belong to the gear effect system because the lowest energy pathway, which provides isochronism of Me groups (the **C** → **D** itinerary), includes a conrotational process.

To make the Me groups isochronous both PSR−disrotation and PSR−conrotation are necessary for olefin **7** and benzene **8** (according to the calculations results no ISR is present for the *tert*-Bu substituents of these compounds). This differs from the case of olefin **9** where a two step PSR − *tert*-Bu rotation − *tert*-Bu rotation (i.e, a triple process with disrotation only) leads to the isochronism of Me groups (see Scheme 3). However, the ISR barrier is found for **9** and it is estimated to be only slightly higher than the concerted process barriers (see Table I). Therefore, conformational dynamics may not be contemplated in terms of securely meshed rotors for this alkene. The most rigid backbone of compound **10** (among the compounds studied) does not undergo distortions during rotation of substituents and hence coupled *tert*-Bu disrotation is a single intramolecular motion in this system.

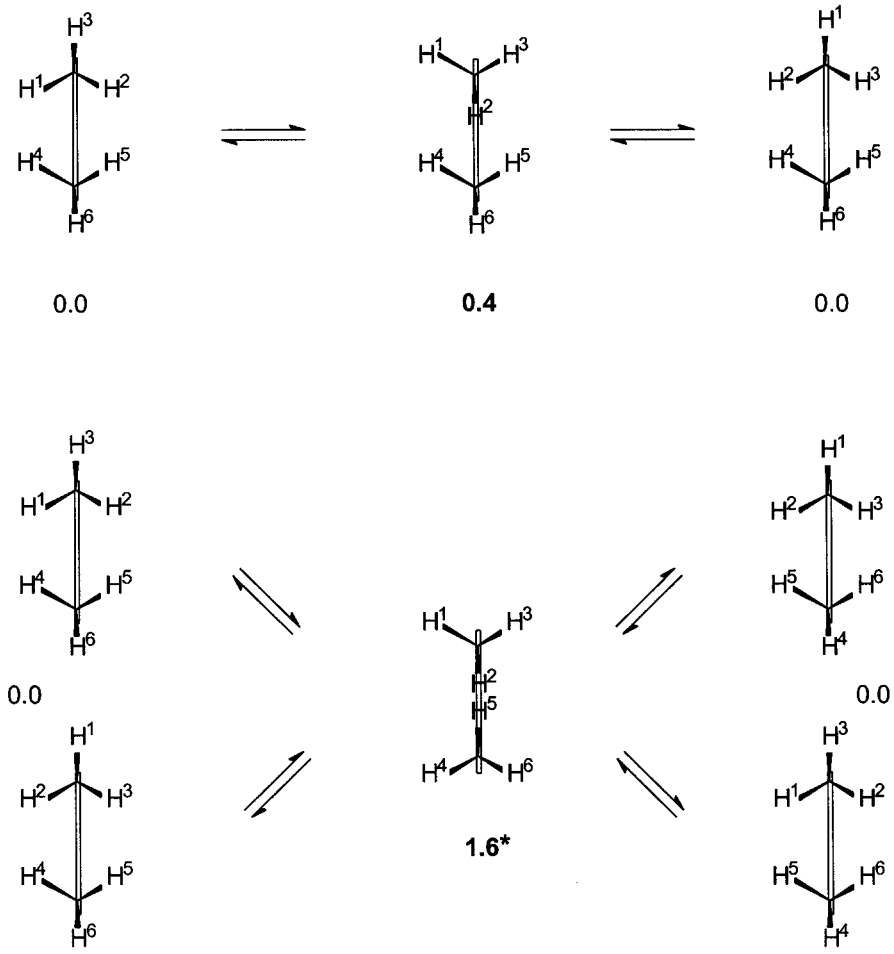
To prove the reliability of the above conclusions for rotation-associated motions we performed the same calculations for 1,2-dimethylbenzene **11**. The rotation of Me groups in this compound was studied by various physical methods and the latest experimental data were consistent with the model of two isolated Me rotors.[22−24] Our results are in agreement with the experimentally deduced model of an isolated threefold Me rotation in the ground state of *o*-xylene: the calculated barrier of ISR (0.4 kcal/mol for the 120° turn; see Scheme 4) is 1.2 kcal/mol lower than that for a concerted rotation (1.6 kcal/mol). The 0.8 kcal/mol difference between the experimental (1.2 kcal/mol, refs. 22 and 23) and the calculated barrier for ISR lies within the limits of usual underestimation of conformational barriers by MM3.[7,8,16] We did not consider other, slightly higher experimental values (see ref. 25 and references therein) because they were extracted via theoretical models based on assumptions of unestimated accuracy.

Thus, vicinal bis-*tert*-Bu derivatives **2**−**4**, **6**, and **10** may be considered as systems with meshed *tert*-Bu rotors (see Table I). Moreover, continuing Mislow's mechanistic analogy,[4] synchronization of particular turns for both *tert*-Bu groups (rotor meshing) and changes of endocyclic torsion angles (backbone deformation) for compounds **2**−**4** and **6** may be classified as meshing of two spur[4] gears on a backbone of low elasticity. Although these *tert*-Bu rotors have no deep notches (which are present for the classical molecular gears of a tripticyl structure[4]), their ''shape friction'' is sufficient to lead to secure conformational transmission of rotation. These compounds provide the first examples of the assistance of additional intramolecular motion to ''pure'' dynamic gearing. Obviously, with an increase of backbone rigidity a concerted triple motion degenerates into a pair of coupled rotations (as in the case of **10**). Concerted PSR−*tert*-Bu conrotation of low energy was found for compounds **4** and **5**; however, it did not lead to isochronism of the Me groups.

Rate-determining barriers (see Table I) in the lowest energy pathways that provide this isochronism are remarkably high for alkanes **2**−**6** (7−10 kcal/mol) and low for olefins **7**, **9**, and **10** (1−3 kcal/mol). Thus, if di-*tert*-Bu substituted saturated systems with low Θ should become available, they will provide experimental proof for PSR assistance to concerted rotation by means of routine DNMR techniques because, according to our results, the rates of these processes lie within the NMR time scale.

## Experimental

The 1994 version of the MM3 program[26] was used for the molecular mechanics calculations. Rotational barriers were calculated using the Drive option of this program. Torsion angles were changed gradually in the range of 0−120 or 150° (2° rotation step) for rotation of both *tert*-Bu groups and in the range of 0−180° (1° rotation step) for rotation of one of the *tert*-Bu groups. Geometry optimization in the regions of the minima and maxima of the steric energy was performed using the full matrix minimization option. A stochastic search followed by full matrix minimization (option 9) was used for locating the transition states and stable conformations. A stochastic search (200 pushes) was performed 3−5 times for each structure starting from different conformations. Coordinates derived from the eigenvectors (produced by option 5 and the Vibplot program) of vibrational modes with negative imaginary frequency were employed as starting coordinates for minimization




**SCHEME 4.** Isolated and concerted rotation of the Me groups in *o*-xylene **11**. Energies (kcal / mol) are relative to the lowest energy conformer. The values for the transition states are shown in bold; the asterisk depicts a second-order transition state.

in the establishment of the formal relationship between conformers and transition states.

## Acknowledgments

A government Eliezer Giladi–Benjamin Fein grant to the first author is gratefully acknowledged. We also thank Dr. P. Aped for his generous assistance.

## References

1. U. Berg, T. Liljefors, C. Roussel, and J. Sandstrom, *Acc. Chem. Res.*, **18**, 80 (1985).
2. J. V. Metzger, M. C. Chanon, and C. M. Roussel, *Rev. Hetrocyc. Chem.*, **15**, 161 (1996).
3. U. Berg and J. Sandstrom, *Adv. Phys. Org. Chem.*, **25**, 1 (1989).
4. K. Mislow, *Chemtracts Org. Chem.*, **2**, 151 (1989).
5. J. V. Metzger, M. C. Chanon, and C. M. Roussel, *Rev. Hetrocyc. Chem.*, **16**, 1 (1997).
6. C. H. Bushweller, In *Acyclic Organonitrogen Stereodynamics*, J. B. Lambert and Y. Takeuchi, Eds., VCH Publishers, New York, 1992, p. 1.
7. A. M. Belostotskii, H. E. Gottlieb, and A. Hassner, *J. Am. Chem. Soc.*, **118**, 7783 (1996).
8. A. M. Belostotskii, P. Aped, and A. Hassner, *J. Mol. Struct. (Theochem.)*, **398–399**, 427 (1997).
9. R. D. Bach and M. Raban, In *Cyclic Organonitrogen Stereodynamics*, J. B. Lambert and Y. Takeuchi, Eds., VCH Publishers, New York, 1992, p. 63.
10. S. F. Nelsen, In *Acyclic Organonitrogen Stereodynamics*; J. B. Lambert and Y. Takeuchi, Eds., VCH Publishers, New York, 1992, p. 89.
11. W. D. Hounshell, L. D. Iroff, D. J. Iverson, R. J. Wroczynski, and K. Mislow, *Isr. J. Chem.*, **20**, 65 (1980).
12. D. T. Dix, G. Fraenkel, H. A. Karnes, and M. S. Newman, *Tetrahedron Lett.*, 517 (1966).
13. M. Raban and D. Kost, In *Acyclic Organonitrogen Stereodynamics*; J. B. Lambert and Y. Takeuchi, Eds., VCH Publishers, New York, 1992, p. 57.

14. W. D. Hounshell, L. D. Iroff, R. J. Wroczynski, and K. Mislow, *J. Am. Chem. Soc.*, **100**, 5212 (1978).
15. R. J. Wroczynski and K. Mislow, *J. Am. Chem. Soc.*, **101**, 3980 (1979).
16. A. M. Belostotskii, P. Aped, and A. Hassner, *J. Mol. Struct.* (*Theochem.*), **429**, 265 (1998).
17. R. Bucourt, *Topics Stereochem.*, **8**, 159 (1974).
18. G. M. Kellie and F. G. Riddel, *Topics Stereochem.*, **8**, 225 (1974).
19. V. M. Andrianov, R. G. Zhbankov, J. V. Krayevsky, and P. Glusinsky, *Bull. Acad. Sci. BSSR*, **33**, 362 (1989).
20. S. F. Nelsen and G. R. Weisman, *J. Am. Chem. Soc.*, **98**, 1842 (1976).
21. A. N. Vereshagin, *Russ. Chem. Rev.*, **52**, 1081 (1983).
22. P. J. Breen, J. A. Warren, and E. R. Bernstein, *J. Am. Chem. Soc.*, **109**, 3453 (1987).
23. P. J. Breen, J. A. Warren, E. R. Bernstein, and J. I. Seeman, *J. Chem. Phys.*, **87**, 1917 (1987).
24. M. Prager, R. Hempelmann, H. Langen, and W. Muller–Warmuth, *J. Phys. Condensed Matter*, **2**, 8625 (1990).
25. R. D. Chirico, S. E. Knipmeyer, A. Nguyen, A. B. Cowell, J. W. Renolds, and W. V. Steele, *J. Chem. Eng. Data*, **42**, 758 (1997).
26. N. L. Allinger, Y. Yuh, and J.-H. Lii, *J. Am. Chem. Soc.*, **111**, 8551 (1989).